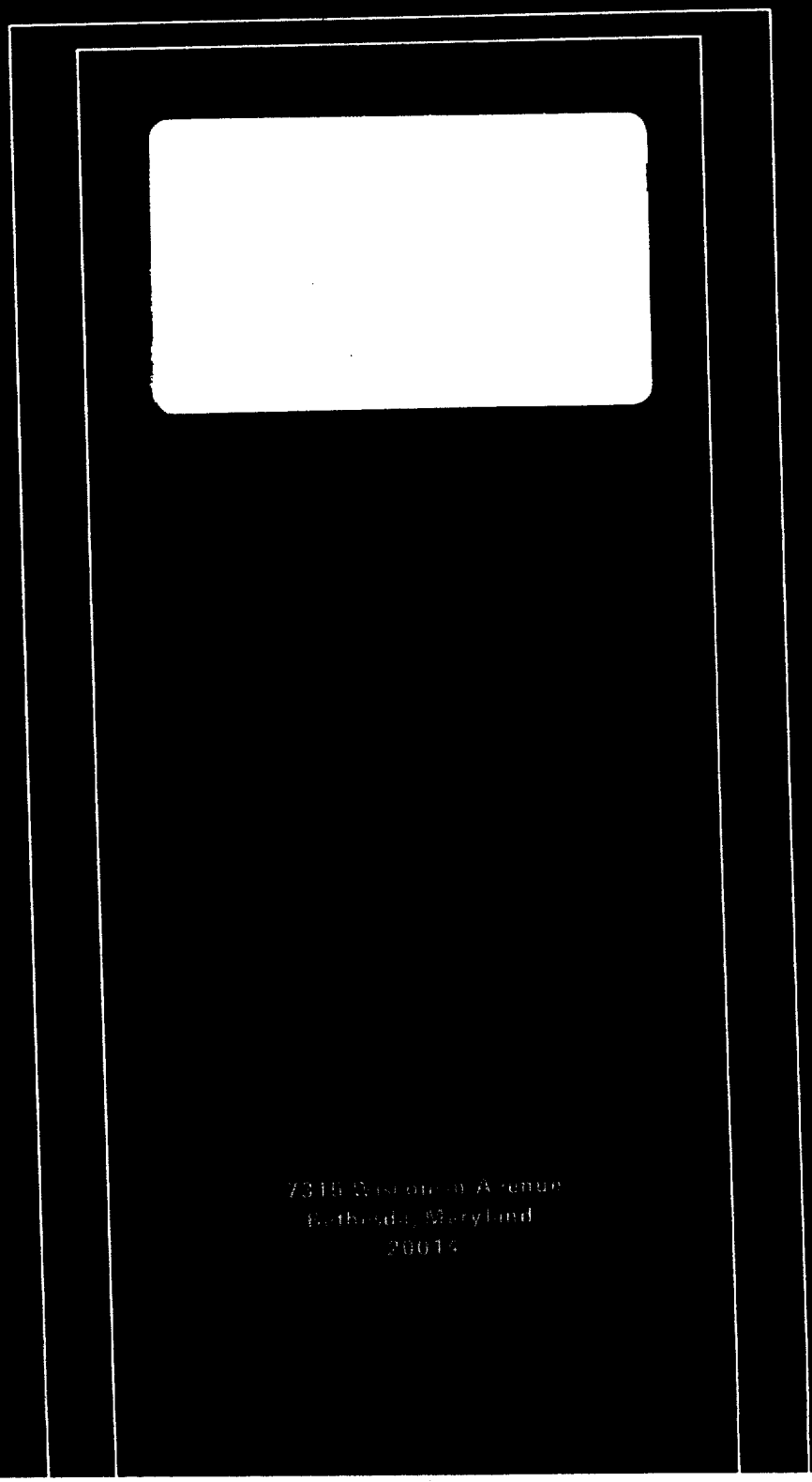
Litton BIONETICS

Mutagenic Evaluation of Compound FDA 73-69 (**Sodium Carboxymethylcellulose**
**Celluose Gum, Low Viscosity**
5/30/75



7315 Wisconsin Avenue
Bethesda, Maryland
20014

LBI PROJECT #2468

# MUTAGENIC EVALUATION OF

# COMPOUND FDA 73-69

PM9004324

SODIUM CARBOXYMETHYLCELLULOSE
CELLULOSE GUM, LOW VISCOSITY

SUBMITTED TO

FOOD & DRUG ADMINISTRATION
DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
ROCKVILLE, MARYLAND

SUBMITTED BY

LITTON BIONETICS, INC.
5516 NICHOLSON LANE
KENSINGTON, MARYLAND

Litton BIONETICS

MAY 30, 1975

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## EVALUATION SUMMARY

Compound FDA 73-69, Sodium Carboxymethylcellulose Cellulose Gum, did not exhibit genetic activity in any of the *in vitro* microbial assays employed in this evaluation.

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DATE: May 30, 1975

SPONSOR: Food and Drug Administration, Contract Number 223-74-2104

SUBJECT: Evaluation of Test Compound PM9004324, Sodium Carboxymethylcellulose Cellulose Gum, Low Viscosity, FDA 73-69

## I. OBJECTIVE

The objective of this study was to evaluate the test compound for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations.

## II. MATERIALS

### A. Test Compound

1. Date Received: August, 1974

2. Description: Fine white powder

### B. Indicator Microorganisms

The following strains of indicator microorganisms were used in the evaluation:

Yeast Strain: *Saccharomyces cerevisiae*, strain D4

Bacteria Strains: *Salmonella typhimurium*, strains: TA-1535
TA-1537
TA-1538

### C. Reaction Mixture

The following reaction mixture was employed in the activation tests:

| Component | Final Concentration/ml |
|---|---|
| 1. TPN (sodium salt) | 6.0 µM |
| 2. Isocitric acid | 49.0 µM |
| 3. Tris buffer, pH 7.4 | 28.0 µM |
| 4. $MgCl_2$ | 1.7 µM |
| 5. Tissue homogenate fraction | 72.0 mg |

D. Tissue Homogenates and Supernatants

The tissue homogenates and 9,000 x g supernatants were prepared from tissues of the following mammalian species: Mouse-ICR random bred adult males; rat-Sprague-Dawley adult males; and primate-Macaca mulatta adult males.

E. Positive Control Compounds

Table 1 lists chemicals for positive controls in the direct and activation assays.

TABLE 1

POSITIVE CONTROLS USED IN DIRECT AND ACTIVATION ASSAYS

| Assay | Chemical[a] | Solvent | Probable Mutagenic Specificity |
|---|---|---|---|
| Nonactivation | Ethyl methanesulfonate | Water or saline | BPS[b] |
| | 2-Nitrofluorene | Dimethylsulfoxide[c] | FS[b] |
| | Quinacrine mustard | Water or saline | FS[b] |
| Activation | Dimethylnitrosamine | Water or saline | BPS[b] |
| | 2-Acetylaminofluorene | Dimethylsulfoxide[c] | FS[b] |

[a] Concentrations given in the Results Section
[b] BPS = base-pair substitution; FS = frameshift
[c] Previously shown to be non-mutagenic

III. METHODS

A. Toxicity

The solubility, toxicity and doses for all chemicals were determined prior to screening.

Each chemical was tested for survival against the specific indicator strains over a range of doses to determine the 50% survival dose. Bacteria were tested in phosphate buffer, pH 7.4, for one hour at 37°C on a shaker. Yeasts were tested in phosphate buffer, pH 7.4, for four hours at 30°C on a shaker. The 50% survival curve and the 1/4 and 1/2 50% doses calculated.

If no toxicity was obtained for a chemical with a given strain, then a maximum dose of 5% (w/v) was used against the strain.

Unless otherwise specified, the doses calculated for the tests in buffer were applied to the activation tests. The solubility of the test chemical under treatment conditions is stated in the Results Section.

B. Plate Tests

In the nonactivation procedure, approximately $10^9$ cells of a log-phase culture of the bacterial indicator strains were spread over the surface of a minimal plate, and a measured amount of the test chemical was placed in the center of the test plate. In activation tests, the test chemical was added to the cells, and an aliquot of the mixture was spread on the surface of the test plate. The reaction mixture (0.1 ml) plus tissue extract was then spotted on the surface of the plate. Positive and solvent controls were included. All plates were incubated at 37°C for four days and then scored. Each compound (test, positive control and solvent control) was done in duplicate. Concentrations of the positive control compounds are listed in the Results Section.

C. Suspension Tests

1. Nonactivation

Log-phase bacteria and stationary-phase yeast cultures of the indicator organisms were grown in complete broth, washed and resuspended in 0.9% saline to densities of $1 \times 10^9$ cells/ml and $5 \times 10^7$ cells/ml, respectively. This constituted the working stock for tests of a group of test chemicals and their respective controls. Tests were conducted in plastic tissue culture plates. Cells plus appropriate volume(s) of the test chemical were added to the wells to give a final volume of 1.5 ml. The solvent replaced the test chemical in the negative controls. Treatment was at 30°C for four hours for yeast tests and at 37°C for one hour for bacterial tests. All flasks were shaken during treatment. Following treatment, the plates were set on ice. Aliquots of cells were removed, diluted in sterile saline (4°C) and plated on the appropriate complete media. Undiluted samples from flasks containing the bacteria were plated on minimal selective medium in reversion experiments. Samples from a $10^{-1}$ dilution of treated cells were plated on the selected media for enumeration of gene conversion with strain D4. Bacterial plates were scored after incubation for 48 hours at 37°C. The yeast plates were incubated at 30°C for 3-5 days before scoring.

2. Activation

Bacteria and yeast cells were grown and prepared as described in the nonactivation tests. Measured amounts of the test and control chemicals plus 0.25 ml of the stock-cell suspension were added to wells of the Linbro plate containing the appropriate tissue fraction and reaction mixture. All flasks (bacteria and yeast) were incubated at 37°C in an oxygen atmosphere with shaking. The treatment times as well as the dilutions, plating procedures and scoring of the plates were the same as described for nonactivation tests.

D. Preparation of Tissue Homogenates and 9,000 x g Cell Fractions

Male animals (sufficient to provide the necessary quantities of tissues) were killed by cranial blow, decapitated and bled. Organs were immediately dissected from the animal using aseptic techniques and placed in ice-cold 0.25 M sucrose buffered with Tris at pH of 7.4. Upon collection of the desired quantity of organs, they were washed twice with fresh buffered sucrose and completely homogenized with a motor-driven homogenizing unit at 4°C. The whole organ homogenate obtained from this step was divided into two samples. One sample was frozen at -80°C and the other was centrifuged for 20 minutes at 9,000 x g in a refrigerated centrifuge. The supernatant from the centrifuged sample was retained and frozen at -80°C. These two frozen samples were used for the activation studies.

E. Data Recording and Reporting

Following the specified incubation periods all population plates were scored by an automatic colony counter and the results from each plate of a set were recorded, in ink, on data processing forms. All minimal or other types of selective media plates were hand scored and the results recorded along with the respective population data. Other relevant experimental data were recorded on experimental definition forms. For bacteria strains the number of colonies recorded from either the population or selective plates represents that number in 1 ml of test suspension plated. The numbers recorded for the yeast strain D4 represent the number in 0.5 ml of test suspension plated. The data were then processed and printed from a computer program.

IV. RESULTS SECTION

A. Solubility Properties of the Test Compound

1. Name or code designation of the test compound: PM9004324
Sodium Carboxymethylcellulose, cellulose gum, low viscosity

2. Test solvent: DMSO

3. Solubility of the test compound under treatment conditions:
Soluble under treatment conditions.

4. Additional comments: fine white powder

B. Toxicity and Dosage Determinations for the Test Compound

1. Test date for toxicity determination: February 11, 1975

2. The 50% survival level was determined for bacteria and yeast indicator organisms by conducting survival curves with the test compound at the following concentrations:

Percent Concentration (w/v or v/v)

5.0
0.5
0.05
0.005
0.0005

3. Concentrations of the test compound used in the mutagenicity tests:

| Dose | Percent Concentration | |
|---|---|---|
| | Bacteria | Yeast |
| 1/4 50% Survival | 2.5 | 0.25 |
| 1/2 50% Survival | 5.0 | 0.50 |
| 50% Survival | 10.0 | 1.00 |
| Plate Tests | 5.0 | -- |

## V. SUMMARY OF TEST RESULTS

### Plate Tests

A. Name or code designation of the test compound: PM9004324

B. Test date: March 29, 1975

C. Concentration of the test compound: 5%

| Test | Species | Tissue | Revertants/Plate TA-1535 1 | TA-1535 2 | TA-1537 1 | TA-1537 2 | TA-1538 1 | TA-1538 2 |
|---|---|---|---|---|---|---|---|---|
| 1. Nonactivation | | | | | | | | |
| Solvent Control | --- | --- | 11 | 20 | 4 | 5 | 15 | 11 |
| Positive Control[a] | --- | --- | $>10^5$ | $>10^5$ | 193 | 207 | 145 | 134 |
| Test Compound | --- | --- | 12 | 4 | 12 | 9 | 6 | 8 |
| 2. Activation | | | | | | | | |
| Negative Control | --- | --- | 7 | 10 | 6 | 3 | 7 | 12 |
| Solvent Control | --- | --- | 20 | 24 | 5 | 9 | 15 | 14 |
| Reaction Mixture Control | --- | --- | 23 | 20 | 7 | 8 | 18 | 16 |
| Positive Control[b] | Mouse | Liver | $>10^3$ | $>10^3$ | 39 | 34 | 343 | 357 |
| Positive Control | | Lung | 12 | 8 | 2 | 1 | 11 | 16 |
| Positive Control | | Testes | 16 | 17 | 3 | 8 | 7 | 11 |
| Positive Control | Rat | Liver | $>10^3$ | $>10^3$ | 89 | 88 | 347 | 341 |
| Positive Control | | Lung | 14 | 7 | 2 | 3 | 14 | 18 |
| Positive Control | | Testes | 16 | 13 | 5 | 7 | 10 | 13 |
| Positive Control | Monkey | Liver | 273 | 356 | 30 | 33 | 123 | 119 |
| Positive Control | | Lung | 8 | 8 | 2 | 2 | 13 | 14 |
| Positive Control | | Testes | 15 | 12 | 3 | 6 | 8 | 11 |
| Test Compound | Mouse | Liver | 3 | 6 | 4 | 4 | 13 | 15 |
| Test Compound | | Lung | 7 | 5 | 2 | 1 | 8 | 8 |
| Test Compound | | Testes | 4 | 7 | 1 | 5 | 10 | 8 |
| Test Compound | Rat | Liver | 4 | 7 | 4 | 2 | 10 | 11 |
| Test Compound | | Lung | 5 | 7 | 4 | 1 | 9 | 4 |
| Test Compound | | Testes | 2 | 5 | 4 | 4 | 13 | 4 |
| Test Compound | Monkey | Liver | 5 | 6 | 4 | 2 | 10 | 8 |
| Test Compound | | Lung | 3 | 5 | 3 | 1 | 12 | 4 |
| Test Compound | | Testes | 4 | 5 | 0 | 4 | 6 | 3 |

a TA-1535 EMS 10 µl/plate
TA-1537 QM 20 µg/plate
TA-1538 NF 100 µg/plate

b TA-1535 DMNA 50 µM/plate
TA-1537 AAF 100 µg/plate
TA-1538 AAF 100 µg/plate

## DATA TABLE TERMS AND ABBREVIATIONS

| ABBREVIATION OR TERM | DEFINITION OR EXPLANATION |
|---|---|
| COMPOUND | Client designated compound number appears in this column. |
| TEST CODES | NAN = Nonactivation: Solvent Control<br>NAP = Nonactivation: Positive Control<br>NA1 = Nonactivation: Test Compound Dose 1<br>NA2, etc. = Reflects the other dose level(s)<br><br>A+C = Negative Chemical Control<br>A-C = Activation: Solvent Control<br>ACP = Activation: Positive Control<br>ACT = Activation: Test Compound<br>A+T = Activation: Tissue Control<br><br>LI = Liver Tissue Activation Fraction<br>LU = Lung Tissue Activation Fraction<br>KI = Kidney Tissue Activation Fraction<br>TE = Testes Tissue Activation Fraction<br>1,2, etc. = Dose Levels |
| CONCENTRATION | All test compound dose levels are expressed as a whole number followed by an exponent (negative) identified by the appropriate units.<br><br>Example: 0025-2PCT = 0.25 percent concentration |
| POPU | Total number of viable cells in the plating sample raised to some exponent printed directly below the abbreviation (i.e., EP + 6 = x $10^6$). |
| MUT 1 | Total number of mutants or convertants obtained from the sample plated raised to some exponent printed directly below the abbreviation (i.e., EP + 0 = x $10^0$). For strain D4, MUT 1 represents the number of ADE+ convertants. |
| MUT 2 | Only used for strain D4 and represents the number of TRY+ convertants in the plated sample. |
| FREQ 1 | The calculated mutation or gene conversion frequency times the negative exponent written directly below. For strain D4, FREQ 1 represents the ADE+ value. |
| FREQ 2 | Only used for strain D4 and represents the TRY+ conversion frequency. |
| CONTAM | Presence of contamination on any plates. |

DATA TABLE TERMS AND ABBREVIATIONS (continued)

| ABBREVIATION OR TERM | DEFINITION OR EXPLANATION |
|---|---|
| AAF | 2-Acetylaminofluorene |
| DMSO | Dimethylsulfoxide |
| DMN | Dimethylnitrosamine |
| EMS | Ethyl Methanesulfonate |
| QM | Quinacrine Mustard |
| NF | Nitrofluorene |
| SPECIES | Animal Strains |
| SPRDAW | Sprague Dawley Rats |
| ICRFLO | Flow ICR Random Bred Mice |
| RHESUS | Rhesus Monkey (Macaca mulatta) |
| MIXEDB | Dog, Mixed Breed |
| NEWZEA | New Zealand White Rabbit |

LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
REPORT EXR34

COMPOUND FREQUENCY SUMMARY REPORT 05/15/75

SPECIES COMPOUND PM9004324

| TEST | ORG | TA1535 HIS EX-8 | TA1537 HIS EX-8 | TA1538 HIS EX-8 | 0000D4 ADE EX-5 | 0000D4 TRY EX-5 |
|---|---|---|---|---|---|---|
| NAN | | 10.15 | 2.10 | 9.02 | 1.58 | 1.69 |
| NAP | | 273.70 | 225.89 | 145.97 | 113.25 | 60.11 |
| NA1 | | 11.49 | 1.33 | 3.31 | 3.12 | 2.63 |
| NA2 | | 17.27 | 2.23 | 6.23 | 1.73 | 1.15 |

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LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
REPORT EXR34

COMPOUND FREQUENCY SUMMARY REPORT 05/15/75

SPECIES ICRFLO COMPOUND PM9004324

| TEST | ORG | TA1535 HIS EX-8 | TA1537 HIS EX-8 | TA1538 HIS EX-8 | 0000D4 ADE EX-5 | 0000D4 TRY EX-5 |
|---|---|---|---|---|---|---|
| ACT | A+C | 5.99 | 2.10 | 11.20 | 16.01 | 4.11 |
| ACT | A+T | 12.45 | 2.10 | 10.46 | 15.24 | 3.26 |
| ACT | A-C | 6.65 | 2.91 | 10.54 | 19.85 | 3.33 |
| ACT | PLI | 1168.86 | 10.07 | 37.43 | 20.62 | 4.92 |
| ACT | PLU | 8.06 | 2.19 | 12.57 | 39.08 | 3.22 |
| ACT | PTE | 9.32 | 2.86 | 12.54 | 23.53 | 3.29 |
| ACT | LI1 | 5.55 | 0.70 | 21.40 | 18.25 | 3.04 |
| ACT | LI2 | 9.21 | 2.52 | 23.47 | 19.47 | 2.81 |
| ACT | LU1 | 3.88 | 2.88 | 11.86 | 13.93 | 2.90 |
| ACT | LU2 | 9.05 | 1.84 | 19.85 | 21.77 | 3.14 |
| ACT | TE1 | 3.81 | 0.69 | 15.94 | 17.86 | 3.57 |
| ACT | TE2 | 8.88 | 1.27 | 14.13 | 21.59 | 3.20 |

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LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
REPORT EXR34

COMPOUND FREQUENCY SUMMARY REPORT 05/15/75

SPECIES SPRDAW COMPOUND PM9004324

| TEST | ORG | TA1535 HIS EX-8 | TA1537 HIS EX-8 | TA1538 HIS EX-8 | 0000D4 ADE EX-5 | 0000D4 TRY EX-5 | 0000D4 ADE EX-5 | 0000D4 TRY EX-5 |
|---|---|---|---|---|---|---|---|---|
| ACT | A+C | 17.47 | 0.63 | 5.39 | 0.58 | 0.39 | | |
| ACT | A+T | 11.03 | 1.23 | 10.55 | 2.35 | 2.75 | | |
| ACT | A-C | 11.62 | 0.58 | 5.36 | 0.72 | 0.18 | 1.14 | 2.12 |
| ACT | PLI | 1500.00 | 7.28 | 59.37 | 8.75 | 10.22 | | |
| ACT | PLU | 18.29 | 0.84 | 7.31 | 3.40 | 1.39 | | |
| ACT | PTE | 22.47 | 0.33 | 8.13 | 3.38 | 1.93 | | |
| ACT | LI1 | 9.85 | 0.37 | 9.57 | 11.16 | 6.47 | 0.48 | 1.77 |
| ACT | LI2 | 9.85 | 0.49 | 11.88 | 2.02 | 3.58 | 0.43 | 1.72 |
| ACT | LU1 | 8.27 | 0.50 | 7.16 | 2.15 | 2.90 | | |
| ACT | LU2 | 15.02 | 0.44 | 6.51 | 3.22 | 2.35 | | |
| ACT | TE1 | 7.69 | 0.35 | 3.31 | 2.46 | 4.06 | | |
| ACT | TE2 | 20.04 | 0.34 | 9.98 | 2.78 | 2.56 | | |

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LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
REPORT EXR34

COMPOUND FREQUENCY SUMMARY REPORT 05/15/75

SPECIES RHESUS COMPOUND PM9004324

| TEST | ORG | TA1535 HIS EX-8 | TA1537 HIS EX-8 | TA1538 HIS EX-8 | 0000D4 ADE EX-5 | 0000D4 TRY EX-5 |
|---|---|---|---|---|---|---|
| ACT | A+C | 7.43 | 7.44 | 4.49 | 10.40 | 1.65 |
| ACT | A+T | 14.05 | 11.84 | 4.09 | 15.69 | 2.55 |
| ACT | A-C | 7.01 | 7.04 | 5.55 | 14.76 | 2.24 |
| ACT | PLI | 1352.79 | 19.31 | 24.13 | 14.99 | 2.71 |
| ACT | PLU | 4.62 | 6.35 | 2.77 | 12.58 | 2.35 |
| ACT | PTE | 8.16 | 8.79 | 6.29 | 20.07 | 2.79 |
| ACT | LI1 | 3.93 | 3.10 | 2.40 | 14.67 | 4.34 |
| ACT | LI2 | 5.80 | 2.19 | 3.33 | 14.13 | 1.94 |
| ACT | LU1 | 3.30 | 1.18 | 2.21 | 18.16 | 1.84 |
| ACT | LU2 | 4.04 | 5.81 | 2.44 | 12.05 | 2.93 |
| ACT | TE1 | 1.74 | 11.90 | 5.45 | 8.22 | 2.63 |
| ACT | TE2 | 4.55 | 7.10 | 6.87 | 11.49 | 3.28 |

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## VI. INTERPRETATION OF RESULTS AND CONCLUSIONS

Compound FDA 73-69, Sodium Carboxymethylcellulose Cellulose Gum, was evaluated for genetic activity in a series of in vitro microbial assays with and without metabolic activation. The following results were obtained:

### A. Salmonella typhimurium

#### 1. Plate tests

At a concentration of 5.0%, this chemical was not mutagenic for the bacterial strains used in direct and activation plate tests.

#### 2. Nonactivation suspension tests

The results of these tests were negative.

#### 3. Activation suspension tests

The results of these tests were negative.

### B. Saccharomyces cerevisiae

#### 1. Activation suspension tests

The results of these tests were negative.

#### 2. Activation suspension tests

The results of these tests were negative. The LI1 and LI2 dose levels with rat tissue were repeated because of an increased response at both loci of the LI1 dose level of the original run. The repeats were negative.

### C. Conclusions

The test compound Sodium Carboxymethylcellulose Cellulose Gum did not exhibit genetic activity in any of the assays employed in this evaluation.

Submitted by:

David Brusick

David Brusick, Ph.D.
Director of Genetics

# APPENDIX

## Tabulation of Data

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 505803 DETECTOR TA1535 SPECIES DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | NAN | | SALINE | 1340 | 0136 | 10.15 | 0 |
| | NAP | | EMS 0.002 % | 1327 | 3632 | 273.70 | 0 |
| PM9004324 | NA1 | | 0005-0 PCT. | 0792 | 0091 | 11.49 | 0 |
| PM9004324 | NA2 | | 0025-1 PCT. | 0805 | 0139 | 17.27 | 2 |

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REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 508301 DETECTOR TA1537 SPECIES DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | NAN | | SALINE | 0713 | 0015 | 2.10 | 0 |
| | NAP | | QM 1.0 UG/ML | 0421 | 0951 | 225.89 | 0 |
| PM9004324 | NA1 | | 0005-0 PCT. | 1126 | 0015 | 1.33 | 0 |
| PM9004324 | NA2 | | 0025-1 PCT. | 0672 | 0015 | 2.23 | 0 |

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 505802 DETECTOR TA1538 SPECIES DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | NAN | | DMSO | 0599 | 0054 | 9.02 | 0 |
| | NAP | | NF 125 UG-ML | 0546 | 0797 | 145.97 | 0 |
| PM9004324 | NA1 | | 0005-0 PCT. | 0483 | 0016 | 3.31 | 0 |
| PM9004324 | NA2 | | 0025-1 PCT. | 0642 | 0040 | 6.23 | 2 |

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REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 505804 DETECTOR 0000D4 SPECIES DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+4 | MUT1 EP+1 | MUT2 EP+1 | FREQ1 EP-5 | FREQ2 EP-5 | CONTAM |
|---|---|---|---|---|---|---|---|---|---|
| | NAN | | SALINE | 0947 | 0015 | 0016 | 1.58 | 1.69 | 0 |
| | NAP | | EMS 1.0 % | 0702 | 0795 | 0422 | 113.25 | 60.11 | 7 |
| PM9004324 | NA1 | | 0005-1 PCT. | 0609 | 0019 | 0016 | 3.12 | 2.63 | 0 |
| PM9004324 | NA2 | | 0025-2 PCT. | 0694 | 0012 | 0008 | 1.73 | 1.15 | 3 |

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REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 506301 DETECTOR TA1535 SPECIES ICRFLO DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | A+C | | DMN 50 UM/ML | 0734 | 0044 | 5.99 | 0 |
| | A+T | | ***NO MATCH*** | 0819 | 0102 | 12.45 | 0 |
| | A-C | | SALINE | 0917 | 0061 | 6.65 | 0 |
| | ACP | LI | DMN 50 UM/ML | 0456 | 5330 | 1168.86 | 1 |
| | ACP | LU | DMN 50 UM/ML | 0608 | 0049 | 8.06 | 0 |
| | ACP | TE | DMN 50 UM/ML | 0590 | 0055 | 9.32 | 0 |
| PM9004324 | ACT | LI1 | 0005-0 PCT. | 1207 | 0067 | 5.55 | 0 |
| PM9004324 | ACT | LI2 | 0025-1 PCT. | 0901 | 0083 | 9.21 | 0 |
| PM9004324 | ACT | LU1 | 0005-0 PCT. | 1004 | 0039 | 3.88 | 0 |
| PM9004324 | ACT | LU2 | 0025-1 PCT. | 0685 | 0062 | 9.05 | 0 |
| PM9004324 | ACT | TE1 | 0005-0 PCT. | 1522 | 0058 | 3.81 | 0 |
| PM9004324 | ACT | TE2 | 0025-1 PCT. | 0912 | 0081 | 8.88 | 0 |

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 505901 DETECTOR TA1537 SPECIES ICRFLO DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | A+C | | AAF 800 UG/ML | 1476 | 0031 | 2.10 | 0 |
| | A+T | | ***NO MATCH*** | 1524 | 0032 | 2.10 | 0 |
| | A-C | | DMSO | 1445 | 0042 | 2.91 | 0 |
| | ACP | LI | AAF 800 UG/ML | 1489 | 0150 | 10.07 | 0 |
| | ACP | LU | AAF 800 UG/ML | 1463 | 0032 | 2.19 | 0 |
| | ACP | TE | AAF 800 UG/ML | 1293 | 0037 | 2.86 | 0 |
| PM9004324 | ACT | LI1 | 0005-0 PCT. | 1424 | 0010 | 0.70 | 2 |
| PM9004324 | ACT | LI2 | 0025-1 PCT. | 1708 | 0043 | 2.52 | 2 |
| PM9004324 | ACT | LU1 | 0005-0 PCT. | 1145 | 0033 | 2.88 | 2 |
| PM9004324 | ACT | LU2 | 0025-1 PCT. | 1522 | 0028 | 1.84 | 0 |
| PM9004324 | ACT | TE1 | 0005-0 PCT. | 3029 | 0021 | 0.69 | 0 |
| PM9004324 | ACT | TE2 | 0025-1 PCT. | 2126 | 0027 | 1.27 | 0 |

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 506401 DETECTOR TA1538 SPECIES ICRFLO DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | A+C | | AAF 800 UG/ML | 0598 | 0067 | 11.20 | 0 |
| | A+T | | ***NO MATCH*** | 0841 | 0088 | 10.46 | 0 |
| | A-C | | DMSO | 0446 | 0047 | 10.54 | 0 |
| | ACP | LI | AAF 800 UG/ML | 0505 | 0189 | 37.43 | 0 |
| | ACP | LU | AAF 800 UG/ML | 0565 | 0071 | 12.57 | 2 |
| | ACP | TE | AAF 800 UG/ML | 0606 | 0076 | 12.54 | 0 |
| PM9004324 | ACT | LI1 | 0005-0 PCT. | 0285 | 0061 | 21.40 | 2 |
| PM9004324 | ACT | LI2 | 0025-1 PCT. | 0294 | 0069 | 23.47 | 2 |
| PM9004324 | ACT | LU1 | 0005-0 PCT. | 0413 | 0049 | 11.86 | 2 |
| PM9004324 | ACT | LU2 | 0025-1 PCT. | 0262 | 0052 | 19.85 | 2 |
| PM9004324 | ACT | TE1 | 0005-0 PCT. | 0251 | 0040 | 15.94 | 0 |
| PM9004324 | ACT | TE2 | 0025-1 PCT. | 0446 | 0063 | 14.13 | 0 |

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 510401 DETECTOR 0000D4 SPECIES ICRFLO DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+4 | MUT1 EP+1 | MUT2 EP+1 | FREQ1 EP-5 | FREQ2 EP-5 | CONTAM |
|---|---|---|---|---|---|---|---|---|---|
| | A+C | | DMN 90 UM/ML | 0706 | 0113 | 0029 | 16.01 | 4.11 | 0 |
| | A+T | | ***NO MATCH*** | 1319 | 0201 | 0043 | 15.24 | 3.26 | 6 |
| | A-C | | SALINE | 0660 | 0131 | 0022 | 19.85 | 3.33 | 2 |
| | ACP | LI | DMN 90 UM/ML | 0325 | 0067 | 0016 | 20.62 | 4.92 | 6 |
| | ACP | LU | DMN 90 UM/ML | 0870 | 0340 | 0028 | 39.08 | 3.22 | 2 |
| | ACP | TE | DMN 90 UM/ML | 0850 | 0200 | 0028 | 23.53 | 3.29 | 4 |
| PM9004324 | ACT | LI1 | 0005-1 PCT. | 0559 | 0102 | 0017 | 18.25 | 3.04 | 2 |
| PM9004324 | ACT | LI2 | 0025-2 PCT. | 0570 | 0111 | 0016 | 19.47 | 2.81 | 6 |
| PM9004324 | ACT | LU1 | 0005-1 PCT. | 0517 | 0072 | 0015 | 13.93 | 2.90 | 4 |
| PM9004324 | ACT | LU2 | 0025-2 PCT. | 0542 | 0118 | 0017 | 21.77 | 3.14 | 0 |
| PM9004324 | ACT | TE1 | 0005-1 PCT. | 0504 | 0090 | 0018 | 17.86 | 3.57 | 6 |
| PM9004324 | ACT | TE2 | 0025-2 PCT. | 0718 | 0155 | 0023 | 21.59 | 3.20 | 6 |

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 506501 DETECTOR TA1535 SPECIES SPRDAW DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | A+C | | DMN 50 UM/ML | 0435 | 0076 | 17.47 | 0 |
| | A+T | | ***NO MATCH*** | 0571 | 0063 | 11.03 | 0 |
| | A-C | | SALINE | 0697 | 0081 | 11.62 | 0 |
| | ACP | LI | DMN 50 UM/ML | 0388 | 5820 | 1500.00 | 0 |
| | ACP | LU | DMN 50 UM/ML | 0410 | 0075 | 18.29 | 0 |
| | ACP | TE | DMN 50 UM/ML | 0356 | 0080 | 22.47 | 2 |
| PM9004324 | ACT | LI1 | 0005-0 PCT. | 0660 | 0065 | 9.85 | 2 |
| PM9004324 | ACT | LI2 | 0025-1 PCT. | 0670 | 0066 | 9.85 | 2 |
| PM9004324 | ACT | LU1 | 0005-0 PCT. | 0762 | 0063 | 8.27 | 0 |
| PM9004324 | ACT | LU2 | 0025-1 PCT. | 0666 | 0100 | 15.02 | 0 |
| PM9004324 | ACT | TE1 | 0005-0 PCT. | 0884 | 0068 | 7.69 | 2 |
| PM9004324 | ACT | TE2 | 0025-1 PCT. | 0544 | 0109 | 20.04 | 1 |

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 507001 DETECTOR TA1537 SPECIES SPRDAW DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | A+C | | AAF 800 UG/ML | 1906 | 0012 | 0.63 | 0 |
| | A+T | | ***NO MATCH*** | 2198 | 0027 | 1.23 | 0 |
| | A-C | | DMSO | 1900 | 0011 | 0.58 | 0 |
| | ACP | LI | AAF 800 UG/ML | 1594 | 0016 | 7.28 | 0 |
| | ACP | LU | AAF 800 UG/ML | 1657 | 0014 | 0.84 | 2 |
| | ACP | TE | AAF 800 UG/ML | 1841 | 0006 | 0.33 | 2 |
| PM9004324 | ACT | LI1 | 0005-0 PCT. | 2449 | 0009 | 0.37 | 0 |
| PM9004324 | ACT | LI2 | 0025-1 PCT. | 1826 | 0009 | 0.49 | 0 |
| PM9004324 | ACT | LU1 | 0005-0 PCT. | 2382 | 0012 | 0.50 | 2 |
| PM9004324 | ACT | LU2 | 0025-1 PCT. | 2255 | 0010 | 0.44 | 0 |
| PM9004324 | ACT | TE1 | 0005-0 PCT. | 2298 | 0008 | 0.35 | 2 |
| PM9004324 | ACT | TE2 | 0025-1 PCT. | 2045 | 0007 | 0.34 | 2 |

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REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 507901 DETECTOR TA1538 SPECIES SPRDAW DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | A+C | | AAF 800 UG/ML | 0445 | 0024 | 5.39 | 0 |
| | A+T | | ***NO MATCH*** | 0275 | 0029 | 10.55 | 2 |
| | A-C | | DMSO | 0392 | 0021 | 5.36 | 0 |
| | ACP | LI | AAF 800 UG/ML | 0507 | 0301 | 59.37 | 0 |
| | ACP | LU | AAF 800 UG/ML | 0588 | 0043 | 7.31 | 0 |
| | ACP | TE | AAF 800 UG/ML | 0541 | 0044 | 8.13 | 0 |
| PM9004324 | ACT | LI1 | 0005-0 PCT. | 0397 | 0038 | 9.57 | 0 |
| PM9004324 | ACT | LI2 | 0025-1 PCT. | 0202 | 0024 | 11.88 | 0 |
| PM9004324 | ACT | LU1 | 0005-0 PCT. | 0335 | 0024 | 7.16 | 0 |
| PM9004324 | ACT | LU2 | 0025-1 PCT. | 0384 | 0025 | 6.51 | 0 |
| PM9004324 | ACT | TE1 | 0005-0 PCT. | 0514 | 0017 | 3.31 | 2 |
| PM9004324 | ACT | TE2 | 0025-1 PCT. | 0451 | 0045 | 9.98 | 2 |

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 506601 DETECTOR 0000D4 SPECIES SPRDAW DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+4 | MUT1 EP+1 | MUT2 EP+1 | FREQ1 EP-5 | FREQ2 EP-5 | CONTAM |
|---|---|---|---|---|---|---|---|---|---|
| | A+C | | DMN 90 UM/ML | 1037 | 0006 | 0004 | 0.58 | 0.39 | 4 |
| | A+T | | ***NO MATCH*** | 1020 | 0024 | 0028 | 2.35 | 2.75 | 4 |
| | A-C | | SALINE | 1104 | 0008 | 0002 | 0.72 | 0.18 | 4 |
| | ACP | LI | DMN 90 UM/ML | 0949 | 0083 | 0097 | 8.75 | 10.22 | 4 |
| | ACP | LU | DMN 90 UM/ML | 0794 | 0027 | 0011 | 3.40 | 1.39 | 6 |
| | ACP | TE | DMN 90 UM/ML | 1035 | 0035 | 0020 | 3.38 | 1.93 | 4 |
| PM9004324 | ACT | LI1 | 0005-1 PCT. | 0726 | 0081 | 0047 | 11.16 | 6.47 | 6 |
| PM9004324 | ACT | LI2 | 0025-2 PCT. | 0893 | 0018 | 0032 | 2.02 | 3.58 | 0 |
| PM9004324 | ACT | LU1 | 0005-1 PCT. | 0792 | 0017 | 0023 | 2.15 | 2.90 | 4 |
| PM9004324 | ACT | LU2 | 0025-2 PCT. | 0807 | 0026 | 0019 | 3.22 | 2.35 | 6 |
| PM9004324 | ACT | TE1 | 0005-1 PCT. | 0812 | 0020 | 0033 | 2.46 | 4.06 | 4 |
| PM9004324 | ACT | TE2 | 0025-2 PCT. | 0900 | 0025 | 0023 | 2.78 | 2.56 | 4 |

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REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 515605 DETECTOR 0000D4 SPECIES SPRDAW/RAT DATE - 06/17/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+4 | MUT1 EP+1 | MUT2 EP+1 | FREQ1 EP-5 | FREQ2 EP-5 | CONTAM |
|---|---|---|---|---|---|---|---|---|---|
| | A-C | | SALINE | 0614 | 0007 | 0013 | 1.14 | 2.12 | 2 |
| PM9004324 | ACT | LI1 | 0005-1 PCT. | 0620 | 0003 | 0011 | 0.48 | 1.77 | 1 |
| PM9004324 | ACT | LI2 | 0025-2 PCT. | 0697 | 0003 | 0012 | 0.43 | 1.72 | 0 |

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 507201 DETECTOR TA1535 SPECIES RHESUS DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | A+C | | DMN 50 UM/ML | 0888 | 0066 | 7.43 | 2 |
| | A+T | | ***NO MATCH*** | 0541 | 0076 | 14.05 | 0 |
| | A-C | | SALINE | 0913 | 0064 | 7.01 | 0 |
| | ACP | LI | DMN 50 UM/ML | 0502 | 6791 | 1352.79 | 0 |
| | ACP | LU | DMN 50 UM/ML | 0823 | 0038 | 4.62 | 0 |
| | ACP | TE | DMN 50 UM/ML | 0625 | 0051 | 8.16 | 0 |
| PM9004324 | ACT | LI1 | 0005-0 PCT. | 1018 | 0040 | 3.93 | 2 |
| PM9004324 | ACT | LI2 | 0025-1 PCT. | 0741 | 0043 | 5.80 | 2 |
| PM9004324 | ACT | LU1 | 0005-0 PCT. | 0879 | 0029 | 3.30 | 0 |
| PM9004324 | ACT | LU2 | 0025-1 PCT. | 0867 | 0035 | 4.04 | 0 |
| PM9004324 | ACT | TE1 | 0005-0 PCT. | 1493 | 0026 | 1.74 | 0 |
| PM9004324 | ACT | TE2 | 0025-1 PCT. | 0923 | 0042 | 4.55 | 2 |

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REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 511401 DETECTOR TA1537 SPECIES RHESUS DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | A+C | | AAF 800 UG/ML | 0847 | 0063 | 7.44 | 2 |
| | A+T | | ***NO MATCH*** | 0515 | 0061 | 11.84 | 0 |
| | A-C | | DMSO | 0710 | 0050 | 7.04 | 0 |
| | ACP | LI | AAF 800 UG/ML | 0844 | 0163 | 19.31 | 0 |
| | ACP | LU | AAF 800 UG/ML | 0914 | 0058 | 6.35 | 0 |
| | ACP | TE | AAF 800 UG/ML | 0842 | 0074 | 8.79 | 0 |
| PM9004324 | ACT | LI1 | 0005-0 PCT. | 0258 | 0008 | 3.10 | 0 |
| PM9004324 | ACT | LI2 | 0025-1 PCT. | 1919 | 0042 | 2.19 | 0 |
| PM9004324 | ACT | LU1 | 0005-0 PCT. | 0934 | 0011 | 1.18 | 0 |
| PM9004324 | ACT | LU2 | 0025-1 PCT. | 1188 | 0069 | 5.81 | 0 |
| PM9004324 | ACT | TE1 | 0005-0 PCT. | 0336 | 0040 | 11.90 | 0 |
| PM9004324 | ACT | TE2 | 0025-1 PCT. | 0563 | 0040 | 7.10 | 0 |

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REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 507601 DETECTOR TA1538 SPECIES RHESUS DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+6 | MUT1 EP+0 | FREQ1 EP-8 | CONTAM |
|---|---|---|---|---|---|---|---|
| | A+C | | AAF 800 UG/ML | 0802 | 0036 | 4.49 | 0 |
| | A+T | | ***NO MATCH*** | 0464 | 0019 | 4.09 | 0 |
| | A-C | | DMSO | 0721 | 0040 | 5.55 | 0 |
| | ACP | LI | AAF 800 UG/ML | 0601 | 0145 | 24.13 | 2 |
| | ACP | LU | AAF 800 UG/ML | 0649 | 0018 | 2.77 | 0 |
| | ACP | TE | AAF 800 UG/ML | 0572 | 0036 | 6.29 | 0 |
| PM9004324 | ACT | LI1 | 0005-0 PCT. | 0584 | 0014 | 2.40 | 0 |
| PM9004324 | ACT | LI2 | 0025-1 PCT. | 0451 | 0015 | 3.33 | 0 |
| PM9004324 | ACT | LU1 | 0005-0 PCT. | 0498 | 0011 | 2.21 | 0 |
| PM9004324 | ACT | LU2 | 0025-1 PCT. | 0532 | 0013 | 2.44 | 2 |
| PM9004324 | ACT | TE1 | 0005-0 PCT. | 0550 | 0030 | 5.45 | 0 |
| PM9004324 | ACT | TE2 | 0025-1 PCT. | 0495 | 0034 | 6.87 | 0 |

Litton BIONETICS

REPORT EXR33 LITTON BIONETICS MUTAGENIC ACTIVITY SYSTEM
COMPOUND SUMMARY BACKUP DETAIL

CONTRACT 22374-2104 PROJECT 02468
EXPERIMENT 510501 DETECTOR 0000D4 SPECIES RHESUS DATE - 05/15/75

| COMPOUND | TEST | ORG ID | CONCENTRATION | POPU EP+4 | MUT1 EP+1 | MUT2 EP+1 | FREQ1 EP-5 | FREQ2 EP-5 | CONTAM |
|---|---|---|---|---|---|---|---|---|---|
| | A+C | | DMN 90 UM/ML | 0423 | 0044 | 0007 | 10.40 | 1.65 | 0 |
| | A+T | | ***NO MATCH*** | 0548 | 0086 | 0014 | 15.69 | 2.55 | 0 |
| | A-C | | SALINE | 0759 | 0112 | 0017 | 14.76 | 2.24 | 0 |
| | ACP | LI | DMN 90 UM/ML | 0774 | 0116 | 0021 | 14.99 | 2.71 | 0 |
| | ACP | LU | DMN 90 UM/ML | 0469 | 0059 | 0011 | 12.58 | 2.35 | 0 |
| | ACP | TE | DMN 90 UM/ML | 0538 | 0108 | 0015 | 20.07 | 2.79 | 0 |
| PM9004324 | ACT | LI1 | 0005-1 PCT. | 0484 | 0071 | 0021 | 14.67 | 4.34 | 0 |
| PM9004324 | ACT | LI2 | 0025-2 PCT. | 0566 | 0080 | 0011 | 14.13 | 1.94 | 0 |
| PM9004324 | ACT | LU1 | 0005-1 PCT. | 0435 | 0079 | 0008 | 18.16 | 1.84 | 0 |
| PM9004324 | ACT | LU2 | 0025-2 PCT. | 0614 | 0074 | 0018 | 12.05 | 2.93 | 0 |
| PM9004324 | ACT | TE1 | 0005-1 PCT. | 0608 | 0050 | 0016 | 8.22 | 2.63 | 0 |
| PM9004324 | ACT | TE2 | 0025-2 PCT. | 0670 | 0077 | 0022 | 11.49 | 3.28 | 0 |